

Intravenous solutions for influencing renal function and for maintenance therapy.

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Abstract

Disclosed is a novel sterile electrolyte intravenous solution comprising essentially physiological concentrations of sodium and other cations and in general higher than physiological concentrations of bicarbonate. The solution is useful for the treatment of altered renal function and prophylactic treatment of a patient to resist onset of altered renal function.

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(54) Intravenous solutions for Influencing renal function and for maintenance therapy.

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D scripti n

The invention relates to the use of aqueous solutions in the preparation of an intravenous medication solution in the treatment of patients suffering from renal dysfunction or renal failure to increase urine volume and stabilize acid-base balance and for follow up maintenance therapy.

An intravenous solution of the invention is more particularly for treating altered renal function or for prophylactically conditioning the kidney to resist that the kidney enters a condition of altered renal function. The term altered renal function as employed herein means a qualitatively and quantitatively depleted or insufficient production of urine, insufficient clearance of metabolic and toxic substances normally cleared by the kidney such as electrolytes, urea, creatinine, phosphates, endogenous and exogenous toxins, pharmaceuticals and their metabolites, a depleted or insufficient ability of the kidney to acidify the urine by excretion of non-volatile or strong acids, or a depleted or insufficient capability of the kidney to produce bicarbonate and thus inability of the kidney to maintain a metabolic acid-base balance within acceptable limits. In such conditions, the therapy normally involves administration of diuretics, preferably loop diuretics, to encourage diuresis.

The intravenous solution of the invention in general finds application in treating patients preliminary to, during and after surgical intervention or any other condition or treatment which may lead to altered renal function.

Examples of treatment with potentially nephrotoxic substances include contrast media, antibiotics, cytostatics, cytotoxic drugs, and immunosuppressive drugs. A wide variety of solutions, some being described as substitution fluids are employed for intravenous administration. Commonly used solutions and their compositions are shown in the following Table I:

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TABLE I

Solution	Solute	Concentrations g/100 ml	(Na ⁺)	Ionic concentration mval/litre (K ⁺) (Ca ²⁺) (Cl ⁻) (HCO ₃ ⁻)
Dextrose in water				...
5.00%	Glucose	5.00
10.00%	Glucose	10.00
Saline				...
Hypotonoc (0.45 %, half normal)	NaCl	0.45	77	77
Isotonic (0.9 %, normal)	NaCl	0.90	154	154
Hyperionic	NaCl	3.00 5.00	513 855	513 855
Dextrose in saline				...
5 % in 0.22 %	Glucose	5.00	38.5	38.5
5 % in 0.45 %	NaCl	0.22
5 % in 0.9 %	Glucose	5.00	77	77
Ringer's	NaCl	0.45 0.90 0.86	154	154
Lactated Ringer's	KCl CaCl ₂ NaCl	0.03 0.03 0.60	147 4	156
Hyperionic sodium bicarbonate (0.6 M)	KCl	0.03	130 0.31 5.95	109 28 595
Hyperionic sodium bicarbonate (0.9 M)	NaHCO ₃	7.50	893	893
Potassium chloride		14.85	...	211 2

Administration of the Dextrose solutions is physiologically equivalent to the administration of distilled water since glucose is rapidly metabolized to CO₂ and H₂O. The Dextrose is however essential to render the solution isotonic and thus avoid hemolysis. The Saline solutions are most commonly administered since most patients in need of treatment are not only water-depleted but also Na⁺ depleted, i.e. salt-depleted.

The plasma Na⁺ concentration can be employed to assist in determining which of the above Dextrose, Saline or Dextrose in Saline solutions is most appropriate. The Dextrose solutions provide a small amount of calories, for example the 5 % Dextrose or 5 % Dextrose in 0.22 % saline is equivalent to 200 kcal per litre of solution.

The Ringer's solutions comprised in the above Table I include physiologic amounts of K⁺ and Ca⁺⁺ in addition to NaCl. The lactated Ringer's solution comprising 28 mEq of lactate per litre (which metabolizes to HCO₃⁻) has a composition close to that of extracellular fluid.

Th hypertonic Sodium bicarbonate solutions are primarily employed in the treatment of metabolic acidosis for example by administration of a 7.5 % or higher solution comprised in 50 ml ampuls, but can be added to other intravenous solutions, however not including th Ringer's solutions since precipitation of the HCO₃⁻ with the Ca⁺⁺ would take plac . Similarly, the Potassium Chloride solution can be added to other intravenous 5 solutions, but care needs to be taken not to intravenously administer any concentrated solution of K⁺ since this can produce an excessive or too rapid increase in plasma concentration of K⁺, which can be fatal.

Other than the above-mentioned hypertonic Sodium bicarbonate solutions, none of the above solutions are known to have any specific influence on kidney function. The hypertonic Sodium bicarbonate solutions on the other hand are normally administered only in limited quantities, at most in quantities sufficient to temporarily correct, normally only in part, a condition of metabolic acidosis. Suggestions to intravenously administer higher quantities of the available Sodium bicarbonate solutions has met with understandable resistance in view particularly of the fact that such solutions are strongly hypertonic and all comprise very much more than or less than physiological amounts of cation solute. Thus, for example the above-mentioned higher concentration 7.5 % Sodium bicarbonate solution available in 50 ml ampuls comprises about 900 mval of Na⁺, 10 and 900 mval of HCO₃⁻ per litre of solution which is neither physiological for Na⁺ nor for HCO₃⁻. In contrast, 15 the normal value for Na⁺ in the blood is from 135 to 146 mval/litre and the normal value for HCO₃⁻ is 22 to 26 mval/litre.

Solutions comprising NaHCO₃, NaCl and KCl disclosed in the literature include the following electrolyte concentrations (mmol/l) :

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	Document	Na ⁺	K ⁺	Cl ⁻	HCO ₃ ⁻
25	DE-A 2358759	75 - 150	5 - 50	75 - 150	5 - 50
	WO-A 8703809	130 - 165	0 - 5	90 - 120	25 - 35
	WO-A 8703808	130 - 145	0 - 4	95 - 110	20 - 55
30	EP-A 177614	135 - 140	0 - 4	106 - 107.5	27.5 - 35
	EP-A 437274	120 - 154	0 - 5	50 - 120	> 30

Regarding the DE-A-2358759 there are in general concerned solutions intended for parenteral replacement of fluids lost as a result of injury or operative intervention. These solutions distinguish over "lactated Ringer's" solution by replacing lactate with bicarbonate, although the concentration of bicarbonate can be as low as 5 mmol/l. which is well below physiological levels. The solutions can comprise as little as 75 mmol/l. of sodium which is also well below physiological levels. The preferred replacement solutions however comprise about physiological levels of sodium, bicarbonate and chloride and in general a high content in potassium of up to 50 mmol/l., i.e. well above physiological levels.

35 WO-A-8703809 is concerned with providing means for separating components of redox active therapeutic aqueous compositions and in general comprise about physiological amounts of Na⁺, Cl⁻ and HCO₃⁻ useful for parenteral administration or peritoneal dialysis.

The type D solutions disclosed in WO-A 8703808 are of a type intended to be employed in hemodialysis or peritoneal dialysis procedures and in general, additional to comprising HCO₃⁻, will comprise lactate.

40 EP-A-177614 is concerned with a process for producing a mixed electrolyte powder for use in bicarbonate dialysis and may contain, in the final hemodialysis solution, slightly greater than physiological levels of HCO₃⁻, up to 35 mmol/l.

45 EP-A 437274 relates to establishing the conditions under which HCO₃⁻ cations and Ca⁺⁺ anions may together remain in solution, which is apparently dependent on pCO₂ values. The solutions are intended for infusion in the treatment of metabolic acidosis of the type which is prevalent in hemodialysis patients and as a dialysis liquid, The HCO₃⁻ content is > 30 mmol/l. but higher values of HCO₃⁻ > 35 mmol/l. are not contemplated.

In the major proportion of cases in which intravenous infusion of fluids is required, the functioning of the 55 kidney of the patient, even if the kidney was initially healthy, may have been or will be altered by a planned medical intervention. For example, renal dysfunction and failure can be a result of heavy injury or massive intervention. Also, however, many patients requiring infusion of fluids, are in any case already suffering from altered or impaired renal function, e.g. because of age or pre-existing disease.

Kidney functions ar inadequate in a large majority of cases and it is an object of the present invention to

provide a novel use of aqueous solutions as defined below in the preparation of intravenous medication solutions in the treatment of patients suffering from renal dysfunction or renal failure to increase urine volume and stabilize acid-base balance and for follow up maintenance therapy. Said intravenous solutions should be able in particular to acidify the urine, i.e. to increase the capacity of the kidney to excrete hydrogen ions and metabolic acids in the urine, and to increase the volume of urine i.e. the excretion of excess water, (along with increased clearance of substances normally entrained in the urine). Furthermore, in general, the solutions of the present invention should serve to correct any systemic acid-base or electrolyte disorders which may be associated with a condition of acute or chronic renal failure or prevention thereof requiring treatment by intravenous infusion of fluids.

In accordance with the invention, it has been established that relatively large quantities of a solution comprising higher than physiological concentrations of HCO_3^- can be intravenously administered provided that the Sodium content of the solution is not significantly different from physiological levels, i.e. not significantly different from about 135 to about 146 mval/litre. Sodium is the most important electrolyte cation and any significant deviation from physiological concentrations as could arise from i.v. administration of any larger quantity of intravenous solution containing more or less than physiological levels of Na^+ may create undesirable and dangerous side effects. Thus, if for example any substantial quantity, say in excess of 200 ml, of the 7.5 % (0.9 M) i.v. sodium bicarbonate solution discussed above were administered to a patient, the patient would tend towards a condition of hypersodemia which has toxic consequences. A condition of hyposodemia similarly can have life endangering consequences so that in general and presuming that the sodium levels in the serum of the patient are within physiological limits, the intravenous solution of the invention comprises a sodium concentration which substantially matches physiological concentrations. On the other hand, as already indicated, the bicarbonate anion concentration in the solution can be very substantially higher than physiological concentrations. However, concentrations of bicarbonate as high as those comprised in known sodium bicarbonate intravenous solutions are not contemplated. The reason is that an excessive or too rapid an increase of bicarbonate in plasma can be fatal as a consequence of systemic alkalosis or hypercapnea (excessive CO_2 concentration arising from decomposition of HCO_3^- into CO_2 and H_2O). Other anions and cations comprised in the intravenous solution of the invention would in general be within or close to physiological levels. Thus, potassium cation would normally be present in the solution at physiological concentrations but could be left away especially if the patient is inclined to hyperkalemia as is sometimes the case. Similarly, chloride anion would be present at physiological levels but can be lower, which latter solution can find use for a patient which is in a condition of hyperchloremic acidosis, as is also sometimes the case.

The intravenous solutions of the invention essentially act on the whole length of the renal nephron-segments, i.e. the renal tubulae, in particular on the proximal tubulae, whereas loop diuretics essentially act on the distal tubulae. A combination of the two effects enables the action of the loop diuretic to be potentiated which can offer means for reducing the dose required, and diuresis to be increased. The supply of bicarbonate contained in the solutions of the invention provide an essential substrate for beneficial conditioning renal function.

An intravenous solution in accordance with the invention comprises at least the following anions and cations, in amounts, i.e. concentrations, within the ranges indicated in the following Table II:

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		mval/litre	(preferably)
	Na^+	130 to 150	135 to 146
45	K^+	0 to 6	2 to 5
	Cl^-	80 to 125	90 to 110
	HCO_3^-	25 to 30 to 70	40 to 60

50 A typical solution useful for treating altered renal function comprises the following amounts and concentrations of electrolytes:

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		mval/litre
Sodium Chloride	5.026 g	Na ⁺ 146
Potassium Chloride	0.298 g	K ⁺ 4
Sodium Bicarbonate	5.040 g	Cl ⁻ 90
Water for infusion solution to 1000.0 ml		HCO_3^- 60

10 Once treatment with a solution such as above has achieved the desired results for a reasonable period, i.e. increased urine volume and stabilized acid-base balance for 24 hours or more, a solution comprising less bicarbonate ions, i.e. less than 40 mval/litre but not lower than physiological levels, i.e. 25 mval/litre may be employed for maintenance therapy. However, since it is important that sodium levels not depart significantly from physiological levels, lowering of the bicarbonate content requires an increase in Sodium Chloride content
 15 which in turn leads to an increase in Chloride content. Hyperchloraemia is often attendant to altered renal function so that increased chloride above physiological levels would in general be avoided.

The dose of intravenous solution administered will of course depend on the weight of the patient, the condition of the patient, specifically the fluid balance, and the effect desired. However, in general, satisfactory results for treating altered renal function and achievement of increased urine volume and associated desired results such as increased clearance of metabolites and toxins, fixed or strong acids, phosphates and the like are obtained when a solution comprising more than about 40 mval/litre of bicarbonate anion is administered at a rate of from 50 to 500 ml of solution/hour (about 15 to 180 drops/min). The total dose required for an adult in twenty-four hours can be as much as 12 litres (= 500 ml/hour). An indication of whether or not the dose is adequate can be obtained by blood gas analysis and by measuring fresh urine pH value. If the urine pH value tends towards or is slightly greater than 7.0, adequate dosage has been achieved. Exemplary clinical trials performed with a bicarbonate-electrolyte solution of the invention are summarized below. The six patients were all urological post-operative patients suffering from prostate or kidney carcinoma.

Diagnosis: Prostate-Carcinoma
 Operation: Radical Lymphadenectomy
 30 Progression: Diuresis: 1st day: 1085 ml
 2nd day: 4130 ml
 3rd day: 5270 ml
 4th day: 4600 ml
 5th day: 1550 ml up to 6 p.m.
 35 (otherwise from 6 a.m. to 6 a.m.)

Infusion program:

1st day:	3000 ml Bicarbonate-electrolyte solution
40	1000 ml Glucose 5 %
2nd day:	2000 ml Combiplasmal 2000 ml Bicarbonate-electrolyte solution + 20 mg Lasix + 40 mval KCl 1000 ml Ringer
3rd day:	2000 ml Bicarbonate-electrolyte solution + 20 mg Lasix + 40 mval KCl
45	2000 ml Combiplasmal 500 ml Glucose 5 % 1000 ml Ringer
4th day:	2000 ml Bicarbonate-electrolyte solution + 20 mg Lasix + 40 mval KCl
50	1000 ml Glucose 5 % 160 ml Combiplasmal 1000 ml Aminosteril 10 % 2000 ml Ringer
5th day:	500 ml Aminosteril 10 % 500 ml Glucose 5 % 1000 ml Ringer
55	1000 ml Bicarbonate-electrolyte solution + 20 mg Lasix + 20 mval KCl infused up to 6 p.m.

Balance:

1st day: 2715 ml
 2nd day: 870 ml
 5 3rd day: 680 ml
 4th day: 1310 ml
 5th day: no balance established

Serum values:

10 1st day: pH 7,37, PCO₂ 39 mmHg, HCO₃ 23 mmol/l, BA - 1,6.
 2nd day: pH 7,42, PCO₂ 42 mmHg, HCO₃ 28 mmol/l, BA + 3,6.
 Urea-N. 27 mg/dl (7-18), Creatinine 2,3 mg/dl, Ca 8,4 mg/dl
 Phosphorous (inorg) 5,5 mg/dl, Protein 5,2 g/dl (other values normal)
 15 3rd day: all values normal except Urea-N. 26 mg/dl, Creatinine 2,0 mg/dl
 Uric acid 8,3 mg/dl, K⁺ 3,2 mmol/l.
 4th day: all values normal except Urea-N. 25 mg/dl, Creatinine 1,6 mg/dl
 K⁺ 3,3 mmol/l, Protein 5,6 g/dl.
 5th day: pH 7,41, PCO₂ 46 mmHg, HCO₃ 29 mmol/l, BA + 4,2.
 20 Urea-N. 33 mg/dl, Creatinine 1,5, mg/dl, K⁺ 3,4 mmol/l,
 Ca 8,5 mg/dl, Protein 5,9 g/dl.

Normal range of Serum values:

25 Blood gas analysis, venous blood:

pH 7,32 - 7,38
 PCO₂ 42 - 50 mmHg
 HCO₃ 23 - 27 mmol/l
 30 BA 0 - + 2,3 mmol/l (BA = base excess / or deficit value)

Serum values:

35 Urea-N 7 - 18 mg/dl
 Creatinine 0,5 - 1,3 mg/dl
 Uric acid 3 - 7 mg/dl
 Phosphorous (inorg) 2,5 - 4,5 mg/dl
 Protein 6,0 - 8,0 g/dl
 40 Na⁺ 135 - 146 mmol/l
 K⁺ 3,5 - 5,0 mmol/l
 Cl⁻ 97 - 108 mmol/l
 Calcium (total) 8,7 - 10,5 mg/dl

Summary:

45 High daily urine volumes, uncomplicated progression. Transferred to General clinic on 5th postoperative day. Adequate control of serum metabolites concentration. Electrolyte and acid-basis-balance essentially normal, mild potassium- and Protein-deficit. Observation period 5 days.

50 Diagnosis:	Kidney-Carcinoma
Operation:	Nephrectomy
Progression: Diuresis:	1st day: 2280 ml 2nd day: 2020 ml 3rd day: 1700 ml (intensive transpiration) 4th day: 2640 ml

Infusion program:

1st day: 2000 ml Bicarbonate-electrolyte solution + 20 mg Lasix + 40 mval KCl
 1000 ml Glucose 5 %

5 2nd day: 1000 ml Glucose 5 %
 2000 ml Bicarbonate-electrolyte solution + 40 mval KCl + 20 mg Lasix

3rd day: 2000 ml Bicarbonate-electrolyte solution + 40 mval KCl + 20 mg Lasix
 1000 ml Glucose 5 %
 500 ml Ringer

10 4th day: 2000 ml Bicarbonate-electrolyte solution + 20 mg Lasix + 40 mval KCl
 1000 ml Glucose 5 %

5th day: 2000 ml Bicarbonate-electrolyte solution + 20 mg Lasix + 40 mval KCl
 1000 ml Glucose 5 %

15 6th day: 1000 ml Bicarbonate-electrolyte solution
 500 ml Glucose 5 %

Balance:

20 1st day: + 570 ml
 2nd day: + 1530 ml
 3rd day: + 1600 ml
 4th day: + 1000 ml
 5th day: + 1300 ml

25 Serum values:

1st day: not determinated

2nd day: Urea-N 19 mg/dl, Creatinine 1,8 mg/dl, Ca 7,8 mg/dl,
 Protein 5,4 g/dl, (other values normal).

30 3rd day: pH 7,45, PCO₂ 45 mmHg, HCO₃ 31 mmol/l, BA + 7,1.

3rd day: Urea-N 34 mg/dl, Creatinine 2,5 mg/dl, Uric-acid 7,6 mg/dl
 Ca 8,1 mg/dl, Protein 5,6 g/dl, (other values normal)

pH 7,49, PCO₂ 40 mmHg, HCO₃ 30 mmol/l, BA + 7,1.

4th day: Urea-N 49 mg/dl, Creatinine 2,4 mg/dl, Ca 7,4 mg/dl,
 Protein 5,2 g/dl, (other values normal)

35 5th day: pH 7,46, PCO₂ 33 mmHg, HCO₃ 23 mmol/l, BA + 1,1.
 Urea-N 46 mg/dl, Creatinine 2,0 mg/dl, Protein 5,6 g/dl,
 Ca 8,0 mg/dl, (other values normal)

6th day: Urea-N 37 mg/dl, Creatinine 1,9 mg/dl, Ca 8,2 mg/dl.

40 Summary:

High daily urine volumes. The observation period ended on the 6th day, when the patient was transferred to the General clinic. In general satisfactory progress. Essentially stabilized acid/base status, including serum concentration of metabolites, electrolytes. Na⁺, K⁺, Cl⁻ always at normal levels.

45 Diagnosis: Prostata-Carcinoma
 Operation: Radical Prostatectomy, Pelvine Lymphadenectomy
 Progression: Diuresis: 1st day: 1380 ml

50 2nd day: 4400 ml
 3rd day: 4100 ml
 4th day: 4250 ml
 5th day: 4450 ml
 6th day: 4100 ml

55 Infusion program:

1st day: 1000 ml Bicarbonate-electrolyte solution

(after 3 p.m.) 1000 ml Glucose 5 %
 1000 ml Ringer
 2nd day: 2000 ml Combiplasmal
 500 ml Lipofundin
 5 500 ml Glucose 5 %
 2000 ml Bicarbonate-electrolyte solution + 20 mg Lasix + 40 mval KCl
 500 ml Glucose 5 %
 3rd day: 2000 ml Bicarbonate-electrolyte solution
 2000 ml Combiplasmal
 10 1000 ml Glucose 5 %
 500 ml Lipofundin
 4th day: 500 ml Lipofundin
 2000 ml Combiplasmal + 20 mval KCl
 2000 ml Bicarbonate-electrolyte solution + 20 mg Lasix + 40 mval KCl
 15 100 ml Humanalbumin
 500 ml Lipofundin
 2000 ml Bicarbonate-electrolyte solution + 20 mg Lasix + 40 mval KCl
 2000 ml Combiplasmal + 20 mval KCl
 500 ml Glucose 5 %
 20 1000 ml Ringer
 6th day: 500 ml Lipofundin
 1000 ml Combiplasmal
 2000 ml Bicarbonate-electrolyte solution + 20 mg Lasix + 40 mval KCl
 500 ml Glucose 5 %
 25 7th day: 500 ml Lipofundin
 500 ml Glucose 5 %
 1000 ml Combiplasmal
 1000 ml Bicarbonate-electrolyte solution + 20 mg Lasix + 20 mval KCl
 all drugs until 12 a.m. then transferred
 30 Balance:
 1st day: + 1670 ml
 2nd day: + 350 ml
 35 3rd day: + 1550 ml
 4th day: + 1120 ml
 5th day: + 2280 ml
 6th day: + 750 ml
 40 Serum values:
 1st day: pH 7,36, PCO₂ 48 mmHg, HCO₃ 27 mmol/l, BA + 1,5.
 2nd day: Protein 4,9 g/dl (6-8), Ca 7,6 mg/dl (8,7-10,5), other values normal.
 pH 7,41, PCO₂ 39 mmHg, HCO₃ 25 mmol/l, BA + 1,3.
 45 3rd day: Potassium 3,4 mmol/l, Protein 4,9 g/dl (6-8),
 pH 7,41, PCO₂ 48 mmHg, HCO₃ 31 mmol/l, BA + 5,6.
 4th day: Potassium 3,3 mmol/l, Ca 7,8 mg/dl, Protein 4,7 g/dl,
 pH 7,43, PCO₂ 39 mmHg, HCO₃ 27 mmol/l, BA + 3,1.
 50 5th day: Potassium 3,5 mmol/l, Ca 8,2 mg/dl, Protein 5,3 g/dl,
 pH 7,42, PCO₂ 42 mmHg, HCO₃ 27 mmol/l, BA + 2,5.
 6th day: Ca 8,0 mg/dl (8,7-10,5), Protein 5,1 g/dl,
 pH 7,42, PCO₂ 42 mmHg, HCO₃ 27 mmol/l, BA + 2,6.
 7th day: Ca 8,1 mg/dl, Protein 5,1 g/dl,
 pH 7,42, PCO₂ 41 mmHg, HCO₃ 27 mmol/l, BA + 2,6.
 55

Summary:

Very high daily urine volumes. Uncomplicated progression, stabilized metabolites, electrolytes and acid-basis-balance, mild potassium-, calcium- and protein-deficit. Transferred to General clinic on 7th postoperative day.

5 Diagnosis: Kidney-Carcinoma
Operation: Nephrectomy
Progression: Diuresis: 1st day: 2760 ml
 2nd day: 620 ml up to 10 a.m.

10 Infusion program:

15 1st day: 1000 ml Bicarbonate-electrolyte solution
 2000 ml Bicarbonate-electrolyte solution + 20 mg Lasix + 40 mval KCl
 500 ml Glucose 5 %
 500 ml Ringer
20 2nd day: 1000 ml Combiplasmal
 1000 ml Bicarbonate-electrolyte solution + 20 mval KCl + 10 mg Lasix
 250 ml Glucose 50 %, up to 10 a.m.

25 Balance:

25 1st day: + 1240 ml
30 2nd day: not evaluated

25 Serum values:

35 1st day: normal
30 2nd day: Protein 4,9 g/dl, Creatinine mg/dl 1,4 mg/dl, Calcium 7,8 mg/dl,
 pH 7,44, PCO₂ 45 mmHg, HCO₃ 30 mmol/l, BA + 6.

Summary:

High daily urine volumes. Uncomplicated progression. Transferred to General clinic on 2nd postoperative day. Stabilized metabolites electrolytes and acid-basis balance. Mild protein- and Ca-deficit.

35 Diagnosis: Kidney-Carcinoma
Operation: Ventral Nephrectomy with Lymphadenectomy
Progression: Diuresis: 1st day: 2800 ml
 2nd day: 2700 ml

40 Infusion program:

45 1st day: 1000 ml Ringer (OP)
 2000 ml Bicarbonate-electrolyte solution + 20 mg Lasix + 40 mval KCl
2nd day: 2000 ml Combiplasmal
 2000 ml Bicarbonate-electrolyte solution + 20 mg Lasix + 40 mval KCl
 500 ml Glucose 5 %

50 Balance:

50 1st day: + 200 ml
55 2nd day: + 1700 ml

55 Serum values:

55 1st day: not evaluated
55 2nd day: normal except Creatinine mg/dl 2,0 mg/dl

pH 7,43, PCO₂ 42 mmHg, HCO₃ 28 mmol/l, BA + 3,9.

Summary:

5 High daily urine volumes. Progression without complications. Observation period 2 days. Metabolites concentration, electrolytes and blood gases essentially normal.

Diagnosis: Stenosis of Urethra, Prostata-Carcinoma, Diab. mellitus

Operation: Pelvine Lymphadenectomy

Progression: Diuresis: 1st day: 2880 ml

10 2nd day: 2200 ml

3rd day: 4030 ml

Infusion program:

15 1st day: 2000 ml Bicarbonate-electrolyte solution, + 20 mg Lasix + 40 mval KCl
1000 ml Glucose 5 %

2nd day: 2000 ml Bicarbonate-electrolyte solution, 40 mval KCl, 20 mg Lasix
1000 ml Glucose 5 %

3rd day: 2000 ml Bicarbonate-electrolyte solution, + 40 mval KCl, 20 mg Lasix

20 4th day: 1000 ml Bicarbonate-electrolyte solution, + 40 mval KCl, 20 mg Lasix

Balance:

1st day: - 470 ml

25 2nd day: + 1490 ml

3rd day: - 530 ml

Serum values:

30 1st day: Urea-N. 21 mg/dl (norm 7-18), Uric acid 8,9 mg/dl (-7)
other values normal

2nd day: mild higher value of Urea N. and Uric acid

Protein 4,9 g/dl (6-8), Ca 7,8 mg/dl (8,7-10,5)

pH 7,41, PCO₂ 49 mmHg, HCO₃ 31 mmol/l, BA + 5,4

35 3rd day: Chloride 96 mmol/l (97-108), Ca. 7,8 mg/dl, Protein 4,9 g/dl
other values normal

pH 7,49, PCO₂ 48 mmHg, HCO₃ 37, BA + 12,5

4th day: Uric acid. 8,9 mg/dl, Potassium 3,4 mmol/l, Ca 8 mg/dl

Phosphorus 2,3 mg/dl (2,5-4,5), Protein 4,9 g/dl

40 other values normal

Summary:

45 High daily urine volumes. Stabilized metabolites, electrolytes-values, Protein mildly lower. Transferred to General clinic on 4th postoperative day = end of observation. Uncomplicated progression.

The components of the solutions may be provided in combined or separated form. Of course, the solutions of the invention may comprise additional substances, such as pharmaceuticals, trace elements, soluble and stable Ca and/or Mg compounds. For example Ca and/or Mg compounds or components may be provided in a container, such as a flexible bag, separate from the bicarbonate component.

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Claims

55 1. Use of an aqueous solution comprising at least the following electrolytes at the concentration indicated below:

mval/l.

5	Na^+	130 to 150
	K^+	0 to 6
	Cl^-	80 to 125
	HCO_3^-	25 to 70

10 in the preparation of an intravenous medication solution in the treatment of patients suffering from renal dysfunction or renal failure to increase urine volume and stabilize acid-base balance.

15 2. The use of an aqueous solution according to claim 1, in which the electrolytes are at the concentrations indicated below:

mval/l.

20	Na^+	135 to 146
	K^+	2 to 5
	Cl^-	90 to 110
25	HCO_3^-	40 to 60

30 3. The use of an aqueous solution according to claim 2, in which the electrolytes are at the concentrations indicated below:

mval/l.

35	Na^+	146
	K^+	4
	Cl^-	90
	HCO_3^-	60

40 4. The use of an aqueous solution according to any one of claims 1 to 3, wherein the treatment is followed by a maintenance therapy using an aqueous solution comprising HCO_3^- in the range of 25 to < 40 mval/l.

45 5. The use of an aqueous solution according to any one of claims 1 to 4, in which the aqueous solutions are provided in conjunction with a solution of a Ca and/or Mg compound.

6. The use of an aqueous solution according to claim 5, in which the solution of the Ca and/or Mg compound is provided in a container, such as a flexible bag, which is separate from the HCO_3^- electrolyte.

7. The use of an aqueous solution according to any one of the claims 1 to 6, in which the therapy involves administration of diuretics to increase diuresis.

8. The use of an aqueous solution according to claim 7, in which the therapy involves administration of loop diuretics to increase diuresis.

Pat entansprüch

1. Verwendung einer wäßrigen Lösung, die zumindest die folgenden Elektrolyte mit den unten angegebenen Konzentrationen umfaßt:

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	mVal/l
Na ⁺	130 bis 150
K ⁺	0 bis 6
Cl ⁻	80 bis 125
HCO ₃ ⁻	25 bis 70

zur Herstellung einer Lösung zur intravenösen Medikation bei der Behandlung von Patienten, die unter Nieren-Dysfunktion oder Nierenversagen leiden, um Urinvolumen zu steigern und das Säure/Base-Gleichgewicht zu stabilisieren.

2. Verwendung einer wäßrigen Lösung nach Anspruch 1, bei welcher die Elektrolyte mit den unten angegebenen Konzentrationen vorliegen:

	mVal/l
Na ⁺	135 bis 146
K ⁺	2 bis 5
Cl ⁻	90 bis 110
HCO ₃ ⁻	40 bis 60

3. Verwendung einer wäßrigen Lösung nach Anspruch 2, bei welcher die Elektrolyte mit den unten angegebenen Konzentrationen vorliegen:

	mVal/l
Na ⁺	146
K ⁺	4
Cl ⁻	90
HCO ₃ ⁻	60

4. Verwendung einer wäßrigen Lösung nach irgendeinem der Ansprüche 1 bis 3, wobei nach der Behandlung eine Aufrechterhaltungstherapie folgt, bei welcher eine wäßrige Lösung verwendet wird, die HCO₃⁻ im Bereich von 25 bis < 40 mVal/l umfaßt.

5. Verwendung einer wäßrigen Lösung nach irgendeinem der Ansprüche 1 bis 4, bei welcher die wäßrigen Lösungen in Verbindung mit einer Lösung einer Ca- und/oder Mg-Verbindung zur Verfügung gestellt werden.

6. Verwendung einer wäßrigen Lösung nach Anspruch 5, bei welcher die Lösung der Ca- und/oder Mg-Verbindung in einem Behälter, wie z.B. einem flexiblen Beutel, welcher vom HCO₃⁻-Elektrolyt getrennt ist, zur Verfügung gestellt wird.

7. Verwendung einer wäßrigen Lösung nach irgendeinem der Ansprüche 1 bis 6, bei welcher die Therapie eine Verabreichung von Diuretika für eine Diuresesteigerung beinhaltet.

8. Verwendung einer wäßrigen Lösung nach Anspruch 7, bei welcher die Therapie eine Verabreichung von

Schleifendiuretika für eine Diuresesteigerung beinhaltet.

Revendicati ns

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1. Utilisation d'une solution aqueuse comprenant au moins l'un des électrolytes suivants à la concentration indiquée ci-dessous :

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	mval/l
Na ⁺	130 à 150
K ⁺	0 à 6
Cl ⁻	80 à 125
HCO ₃ ⁻	25 à 70

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dans la préparation d'une solution de médication intraveineuse dans le traitement de patients souffrant de dysfonctionnement rénal ou de défaillance rénale à augmenter le volume d'urine et à stabiliser l'équilibre acide-base.

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2. Utilisation d'une solution aqueuse selon la revendication 1, dans laquelle les électrolytes sont aux concentrations indiquées ci-dessous :

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	mval/l
Na ⁺	135 à 146
K ⁺	2 à 5
Cl ⁻	90 à 110
HCO ₃ ⁻	40 à 60

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3. Utilisation d'une solution aqueuse selon la revendication 2, dans laquelle les électrolytes sont aux concentrations indiquées ci-dessous :

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	mval/l
Na ⁺	146
K ⁺	4
Cl ⁻	90
HCO ₃ ⁻	60

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4. Utilisation d'une solution aqueuse selon l'une quelconque des revendications 1 à 3, dans lequel le traitement est suivi d'une thérapie de maintien utilisant une solution aqueuse comprenant HCO₃⁻ dans l'intervalle de 25 à < 40 mval/l.

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5. Utilisation d'une solution aqueuse selon l'une quelconque des revendications 1 à 4, dans laquelle les solutions aqueuses sont fournies conjointement avec une solution d'un composé Ca et/ou Mg.

6. Utilisation d'une solution aqueuse selon la revendication 5, dans laquelle la solution d'un composé Ca et/ou Mg est fournie dans un récipient, comme un sac souple, qui est séparé de l'électrolyte HCO₃⁻.

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7. Utilisation d'une solution aqueuse selon l'une quelconque des revendications 1 à 6, dans laquelle la thérapie implique l'administration de diurétiques pour augmenter la diurèse.

- 8. Utilisation d'un solution aqueuse selon la revendication 7, dans laquelle la thérapie implique l'administration de diurétiques de l'anse pour augmenter la diurèse.**

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